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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,453	07/18/2006	Matthew David Osborne	BJS-620-412	4519

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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
07/22/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)
	10/567,453	OSBORNE ET AL.
	Examiner	**Art Unit**
	MARIA MARVICH	1633

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 July 2011 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,4,9,10,13-16,33,36,41 and 45-50*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
    See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Maria B Marvich/
Primary Examiner, Art Unit 1633

Continuation of 11. does NOT place the application in condition for allowance because: Applicants traverse the rejection under 35 USC 103 for the following reasons. Applicants argue that hybridoma cells when cultured under agitation and increased FAC are destroyed and one would not raise the concentration of FAC for myeloma cells as one would expect the same results for myeloma cells. As well, applicants argue that Gorfien found it essential to mitigate the known toxic effects of high iron by using beta glycerophosphate. It is noted that the statement "the person skilled in the art would expect myeloma cells to react in the same way as demonstrated by Field et al for hybridoma cells" cannot be attributed to the examiner. This statement is first stated by applicants. The action in fact pointed out this statement and commented "if hybridoma cells represent the state of the art with myeloma cells than Fields et al teaches that in concentrations embracing those of the instant claims hybridoma cells survive with Fe2+ to about 8 mg/L, however, growth is improved between 0.1 and 1.5 mg/L". To this end and in response to applicants arguments that Fields teaches that increasing FAC under agitation leads to cell destruction (Figure 2B), the specification teaches that "FIG. 2A shows that increasing concentrations of ferric ammonium citrate up to 10 mg/L support increasing cell concentrations in transferrin-free medium in static culture. However, FIG 2B demonstrates that in agitated culture (reciprocal shaking platform) that ferric ammonium citrate concentrations of > 1mg/L are toxic in both the presence and absence of transferrin. While applicants have suggested that hybridoma results can be extrapolated to those of myeloma cells, these results are not the same as those of myeloma cells.
However, the rejection is based upon the methods of Gorfien et al wherein the source of iron is FAC. Gorfien teaches every aspect of the instant method except that the source of the iron is FAC. Specifically, Gorfien et al teaches growth of myeloma cells in media that lacks transferrin, a lipophilic chelator, a synthetic nitrogen-containing chelator or a lipophilic synthetic nitrogen containing chelator. The cells are grown under conditions of agitation in shaker rollers.

[0166] For suspension cultivation, cells are typically suspended in the present culture media and introduced into a culture vessel that facilitates cultivation of the cells in suspension, such as a spinner flask, perfusion apparatus, or bioreactor (see Freshney, R. I., Culture of Animal Cells: A Manual of Basic Technique, New York: Alan R. Liss, Inc., pp. 123-125 (1983)). Ideally, agitation of the media and the suspended cells will be minimized to avoid denaturation of media components and shearing of the cells during cultivation.

Applicants focus solely on 2 cell types to be used in the methods,
[0158] 293 human embryonic kidney cells and HeLaS3 cells are particularly preferred for growth in the suspension medium of the present invention. Chinese hamster ovary (CHO) cells, NS/O cells, and hybridoma cells are particularly preferred for growth in the replacement medium of the present invention. Especially preferred are CHO cells.
Replacement media uses an iron chelate. This is the media of the instant invention. To this end, Gorfien et al teaches use of iron at a concentration of 0.28mg/l to 11 mg/l. The only aspect of Gorfien et al that is lacking is naming as an iron source ferric ammonium citrate. In fact, in Gorfien et al, the exact particulars of the replacement compound do not appear to be limiting. Gorfien teaches
[0113] Fe.sup.2+ and/or Fe.sup.3+ chelate compounds which may be used include but are not limited to compounds containing an Fe.sup.2+ and/or Fe.sup.3+ salt and a chelator such as ethylenediaminetetraacetic acid (EDTA), ethylene glycol-bis(.beta.-aminoethyl ether)-N,N,N,N'-tetraacetic acid (EGTA), deferoxamine mesylate, dimercaptopropanol, diethylenetriaminepentaacetic acid (DPTA), and trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (CDTA). For example, the iron chelate compound may be a ferric citrate chelate or a ferrous sulfate chelate. Preferably, the iron chelate compound used is ferrous sulphate.7H.sub.2O EDTA (FeSO.sub.40.7H.sub.2O EDTA, e.g., Sigma F0518, Sigma, St. Louis, Mo.). In the medium of the present invention, the concentration of Fe.sup.2' and/or Fe.sup.3+ can be optimized using only routine experimentation. Typically, the concentration of Fe.sup.2+ and/or Fe.sup.3+ in the 1.times. medium of the present invention can be about 0.00028 to 0.011 g/L. Preferably, the concentration of iron is about 0.0011 g/L.

A review of the art demonstrates that iron replacements comprise a number of formulations that are used interchangeably and these include the indication that ferric ammonium citrate is a ferric citrate chelator. In other words, ferric ammonium chelate appears to be a ferric citrate chelate by name absent evidence to the contrary. Hence, Fields et al provides description of those items encompassed by but not explicitly disclosed by Gorfien et al.

Hence, the basis of the rejection is that Gorfien et al teaches the instant method but does not provide the details of the iron chelator whereas Fields et al teaches that FAC can serve as an iron chelator in growth of myeloma cells. One would looking at the methods of Gorfien et al be motivated to sue FAC as Gorfien et al directs one to ferric citrate chelators in the methods of growing myeloma cells. The failures of Fields et al are not demonstrated to be due to use of FAC but most presumably by differences in the methods of Fields et al and Gorfien et al. To this end, applicants argue that Gorfien et al teach use of beta glycerophosphate which is not excluded by the instant claims.